```
le medline

COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         0.15       0.15

FILE 'MEDLINE' ENTERED AT 17:37:45 ON 14 DEC 2001

 FILE LAST UPDATED: 13 DEC 2001 (20011213/UP).  FILE COVERS 1958 TO DATE.

 On April 22, 2001, MEDLINE was reloaded.  See HELP RLOAD for details.

 MEDLINE now contains IN-PROCESS records.  See HELP CONTENT for details.

 MEDLINE is now updated 4 times per week.  A new current-awareness alert
 frequency (EVERYUPDATE) is available.  See HELP UPDATE for more information.

 MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
 MeSH 2001 vocabulary.  Enter HELP THESAURUS for details.

 The OLDMEDLINE file segment now contains data from 1958 through 1965.
 Enter HELP CONTENT for details.

 Left, right, and simultaneous left and right truncation are available in the
 Basic Index.  See HELP SFIELDS for details.

 THIS FILE CONTAINS CAS REGISTRY NUMBERS FOR EASY AND ACCURATE
 SUBSTANCE IDENTIFICATION.

=> s (E1 gene)

'E1' NOT FOUND
The E# entered is not currently defined.

=> s E2A

L1          554 E2A

=> s E1

'E1' NOT FOUND
The E# entered is not currently defined.

=> s e1

'E1' NOT FOUND
The E# entered is not currently defined.

=> s (adenovir? E1 gene)

'E1' NOT FOUND
The E# entered is not currently defined.

=> s (embryonic retinoblast?)

         53417 EMBRYONIC
          9306 RETINOBLAST?
L2           3 (EMBRYONIC RETINOBLAST?)
                 (EMBRYONIC(W)RETINOBLAST?)
```

```
=> s l2 and l1

L3            0 L2 AND L1

=> s adenovir? and l1

         22834 ADENOVIR?
L4         191 ADENOVIR? AND L1

=> s retinoblast?

L5        9306 RETINOBLAST?

=> s l5 and l4

L6            9 L5 AND L4

=> s hemagglutinin

L7        6345 HEMAGGLUTININ

=> s haemagglutinin

L8        1721 HAEMAGGLUTININ

=> s l7 and l6

L9            0 L7 AND L6

=> s l8 and l6

L10           0 L8 AND L6

=> d l6 1-9 bib, ab


L6   ANSWER 1 OF 9     MEDLINE
AN   2001237347     MEDLINE
DN   21214592   PubMed ID: 11313936
TI   The p107 tumor suppressor induces stable E2F DNA binding to repress
target
     promoters.
AU   O'Connor R J; Schaley J E; Feeney G; Hearing P
CS   Department of Molecular Genetics and Microbiology, School of Medicine,
     State University of New York, Stony Brook, New York, NY 11794, USA.
NC   CA09176 (NCI)
     CA28146 (NCI)
SO   ONCOGENE, (2001 Apr 5) 20 (15) 1882-91.
     Journal code: ONC; 8711562. ISSN: 0950-9232.
CY   England: United Kingdom
DT   Journal; Article; (JOURNAL ARTICLE)
LA   English
FS   Priority Journals
EM   200105
ED   Entered STN: 20010517
     Last Updated on STN: 20010517
     Entered Medline: 20010503
AB   E2F transcription factors are key players in the regulation of
     proliferation, apoptosis, and differentiation in mammalian cells. E2Fs
are
     negatively regulated by members of the retinoblastoma protein
     family, Rb, p107 and p130. During adenovirus infection, viral
     proteins are expressed that displace Rb family members from E2Fs and
     recruit E2F complexes to viral and cellular promoter regions. This
```

recruitment of E2F involves the induction of stable E2F binding to inverted E2F binding sites in the Ad **E2a** and cellular E2F-1 promoters and induces both viral and cellular gene expression. The cellular p107 tumor suppressor also displays such regulation of E2F DNA binding activity. p107 induces stable E2F-4/DP binding to inverted E2F binding sites in the Ad **E2a** and cellular E2F-1 promoters. The induction of E2F DNA binding by p107 minimally requires the sequences in p107 that mediate E2F interaction. The related tumor suppressor, p130, also effects this function. p107 levels increase substantially as cells progress through S phase. p107 induction of E2F DNA binding was observed primarily in S phase cells coincident with the increase in p107 protein levels. The results of promoter activity assays directly correlate the induction of E2F DNA binding by p107 with effective transcriptional repression. These results support a model in which p107 and p130 induce the stable binding of E2F complexes to promoters that drive expression of critical regulatory proteins such as E2F-1. Since p107 and p130 bind histone deacetylase complexes (HDACs) which repress promoter activity, p107-E2F and p130-E2F would stably recruit repressor complexes to effect efficient promoter repression.

L6 ANSWER 2 OF 9 MEDLINE
AN 2000387818 MEDLINE
DN 20304972 PubMed ID: 10846061
TI The E4-6/7 protein functionally compensates for the loss of E1A expression in **adenovirus** infection.
AU O'Connor R J; Hearing P
CS Department of Molecular Genetics and Microbiology, School of Medicine, State University of New York, Stony Brook 11794, USA.
NC AI41636 (NIAID)
CA09176 (NCI)
CA28146 (NCI)
SO JOURNAL OF VIROLOGY, (2000 Jul) 74 (13) 5819-24.
Journal code: KCV; 0113724. ISSN: 0022-538X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200008
ED Entered STN: 20000818
Last Updated on STN: 20000818
Entered Medline: 20000810
AB The E1A gene products are required and sufficient for activation of **adenovirus** gene expression in cultured cells. The E4-6/7 gene product induces the binding of the cellular transcription factor E2F to the viral **E2a** promoter region. The induction of E2F binding to the **E2a** promoter in vitro is directly correlated with transcriptional activation of the **E2a** promoter in vivo. The E2 region encodes the viral replication proteins, yet **adenoviruses** lacking E4-6/7 function demonstrate no defective phenotype in infected cells. Here we show that the E4-6/7 protein can functionally compensate for E1A expression in virus infection. In the absence of the E1A gene products, expression of the E4-6/7 protein is sufficient to displace **retinoblastoma** protein family members from E2Fs, activate expression of early region 2 via induction of E2F DNA binding to the **E2a** promoter region, and significantly enhance replication of an E1A-defective **adenovirus**. These results have implications in the regulation of viral gene expression and for the development of recombinant **adenovirus** vectors.

L6 ANSWER 3 OF 9 MEDLINE
AN 2000027235 MEDLINE
DN 20027235 PubMed ID: 10559324
TI Induction of transformation and p53-dependent apoptosis by

adenovirus type 5 E4orf6/7 cDNA.
AU Yamano S; Tokino T; Yasuda M; Kaneuchi M; Takahashi M; Niitsu Y; Fujinaga K; Yamashita T
CS Department of Molecular Biology, Cancer Research Institute, Sapporo Medical University School of Medicine, Chuo-ku, Japan.
SO JOURNAL OF VIROLOGY, (1999 Dec) 73 (12) 10095-103.
Journal code: KCV; 0113724. ISSN: 0022-538X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199912
ED Entered STN: 20000113
Last Updated on STN: 20000113
Entered Medline: 19991220
AB **Adenovirus** (Ad) E4orf6/7, one of the early gene products of human Ads, forms a stable complex with the cellular transcription factor E2F to activate transcription from the Ad E2 promoter. E2F cDNAs have growth-promoting and apoptosis-inducing activities when overexpressed in cells. We cloned Ad5 E4orf6/7 cDNA in both simian virus 40- and human cytomegalovirus-based expression vectors to examine its transforming and apoptotic activities. The cloned E4orf6/7 collaborated with a **retinoblastoma** protein (RB)-nonbinding and therefore E2F-nonreleasing mutant of Ad5 E1A (dl922/947) to morphologically transform primary rat cells, suggesting that E2F is an important cellular protein functioning downstream of E1A for transformation. In a G418 colony formation assay, E4orf6/7 was shown to suppress growth of untransformed rat cells. Moreover, a recombinant Ad expressing Ad5 E4orf6/7 induced apoptosis in rat cells when coinfected with wild-type p53-expressing Ad. Mutational analysis of E4orf6/7 revealed that both of the domains required for growth inhibition and transformation by E4orf6/7 lay in the C-terminal region, which is essential for transactivation from the upstream sequence of an **E2a** promoter containing E2F-binding sites. However, the smallest mutant of E4orf6/7, encoding the C-terminal 59 amino acids, failed to complement the RB-nonbinding dl922/947 mutant despite showing growth inhibition and E2F transactivation activities. Thus, it is suggested that a subregion of E4orf6/7 which is required for growth inhibition and transformation in collaboration with dl922/947 overlaps the transactivation domain of E4orf6/7.

L6 ANSWER 4 OF 9 MEDLINE
AN 1998393689 MEDLINE
DN 98393689 PubMed ID: 9724748
TI Suppression of **adenovirus** E1A-induced apoptosis by mutated p53 is overcome by coexpression with Id proteins.
AU Nakajima T; Yageta M; Shiotsu K; Morita K; Suzuki M; Tomooka Y; Oda K
CS Department of Biological Science and Technology, Science University of Tokyo, Noda-shi, Chiba 278, Japan.
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1998 Sep 1) 95 (18) 10590-5.
Journal code: PV3; 7505876. ISSN: 0027-8424.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199809
ED Entered STN: 19981008
Last Updated on STN: 19981008
Entered Medline: 19980928
AB The rat 3Y1 derivative cell lines, EId10 and EId23, established by introducing the **adenovirus** E1A12S, Id-1H, and Id-2H cDNAs linked

to the hormone-inducible promoter, express these proteins upon treatment with dexamethasone and elicit apoptosis, although these cell lines express mutated p53. The E1A mutants containing a deletion in either the N terminus or the conserved region 1 were unable to induce apoptosis in cooperation with Ids. Western blot analysis of the immunoprecipitates prepared from the dexamethasone-treated EId10 cell extract showed that Id-2H preferentially binds to E1A and **E2A** (E12/E47) helix-loop-helix transcription factors in vivo, but scarcely to the **retinoblastoma** protein. After induction of E1A and Ids, EId10 and EId23 cells began to accumulate in S phase and undergo apoptosis before entering G2 phase, suggesting that abnormal synthesis of DNA induced by coexpression of E1A, Id-1H, and Id-2H results in the induction of apoptosis. Apoptosis also is induced in mouse A40 (p53-/-) cells by E1A alone or E1A plus Ids after transient transfection of the expression vectors. The induction of apoptosis is stimulated by coexpression with wild-type p53; however, apoptosis induced by E1A alone was suppressed completely by coexpression with mutated p53, whereas apoptosis induced by E1A plus Ids was stimulated by the mutated p53 as done by wild-type p53. These results suggest that the suppressive function of mutated p53 is overcome by Ids.

L6 ANSWER 5 OF 9 MEDLINE
AN 95018591 MEDLINE
DN 95018591 PubMed ID: 7933066
TI Mutually exclusive interaction of the **adenovirus** E4-6/7 protein and the **retinoblastoma** gene product with internal domains of E2F-1 and DP-1.
AU O'Connor R J; Hearing P
CS Department of Molecular Genetics and Microbiology, State University of New York, Stony Brook 11794.
NC CA09176 (NCI)
CA28146 (NCI)
SO JOURNAL OF VIROLOGY, (1994 Nov) 68 (11) 6848-62.
Journal code: KCV; 0113724. ISSN: 0022-538X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199411
ED Entered STN: 19941222
Last Updated on STN: 19941222
Entered Medline: 19941117
AB The binding of E2F to the **adenovirus** (Ad) **E2a** promoter is stimulated by the Ad E4-6/7 protein. E2F DNA binding activity is composed of a heterodimer of related but distinct proteins of the E2F-1 and DP-1 families. The E4-6/7 protein induces the cooperative and stable binding of E2F to an inverted repeat binding site in the **E2a** promoter apparently by providing a dimerization interface to two adjacent E2F heterodimers. The product of the **retinoblastoma** gene product (Rb) represses the transcriptional activity of E2F by direct protein-protein interaction. In this report, we have examined the regions of E2F-1 and DP-1 that are required for the induction of cooperative E2F binding to the **E2a** promoter by the E4-6/7 protein. Our results demonstrate that an internal segment of E2F-1, that is conserved among members of the E2F family, is required for functional interaction with the E4-6/7 product. Consistent with this observation, other members of the E2F family (E2F-2 and E2F-3) productively interact with E4-6/7. DP-1 also is necessary for stable interaction with E4-6/7 and an internal segment of DP-1 is required that is positioned in a location similar to that of the conserved E2F-1 domain. Interestingly, the binding of E4-6/7 and the binding of Rb to E2F are mutually exclusive, and our results show that the

same internal segments of E2F-1 and DP-1 that are required for E4-6/7 binding are also required for stable interaction with Rb. These results suggest that the Ad E4-6/7 protein mimics Rb in part for the protein interaction requirements for E2F binding, although with different functional consequences. While Rb binding represses E2F activity, the E4-6/7 protein stimulates transactivation of the Ad **E2a** promoter.

L6 ANSWER 6 OF 9 MEDLINE
AN 94047393 MEDLINE
DN 94047393 PubMed ID: 8230491
TI Multiple, distinct trans-activation functions are encoded by the simian virus 40 large T and small t antigens, only some of which require the 82-residue amino-terminal common domain.
AU Loeken M R
CS Joslin Diabetes Center, Boston, Massachusetts.
NC CA50599 (NCI)
SO JOURNAL OF VIROLOGY, (1993 Dec) 67 (12) 7684-9.
Journal code: KCV; 0113724. ISSN: 0022-538X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199312
ED Entered STN: 19940117
Last Updated on STN: 19970203
Entered Medline: 19931221
AB Simian virus 40 (SV40) small t and large T antigens can each trans activate the **adenovirus** (Ad) **E2A** and the Ad VA-I promoters. The first 82 amino acids of large T and small t are identical. However, this large T-small t common domain between residues 1 and 82 does not trans activate, suggesting that large T and small t each encode separate trans-activation functions. To determine whether the large T or small t unique domains, which are required for trans activation of the **E2A** promoter, are sufficient for this activity, we have employed expression plasmids separately encoding the common and unique domains of large T and small t. Cotransfection of a large T unique domain expression plasmid efficiently trans activated the **E2A** promoter. Optimal trans activation by large T required the motif that binds cellular proteins such as the **retinoblastoma** gene product, which is located in the large T unique domain, and additional large T structures outside this motif. In contrast, the small t unique domain did not trans activate the **E2A** promoter. Experiments utilizing **E2A** promoter mutants containing only the ATF- or EIIF-binding sites demonstrated that trans activation by small t involves only the EIIF transcription factor and that this function requires both the common (residues 1 to 82) and the small t unique domains expressed as a colinear protein. trans activation by large T, in contrast, involves at least three mechanisms. There appear to be at least two mechanisms that involve the EIIF transcription factor, at least one of which does not require the common domain (residues 1 to 82) and one mechanism that involves the ATF factor and does require both the common and the large T unique domains.

L6 ANSWER 7 OF 9 MEDLINE
AN 94020820 MEDLINE
DN 94020820 PubMed ID: 8414500
TI Rb may act as a transcriptional co-activator in undifferentiated F9 cells.
CM Erratum in: Oncogene 1994 Mar;9(3):999
AU Bocco J L; Reimund B; Chatton B; Kedinger C
CS Laboratoire de Genetique Moleculaire des Eucaryotes (CNRS), Unite 184 (INSERM), Strasbourg, France.
SO ONCOGENE, (1993 Nov) 8 (11) 2977-86.

Journal code: ONC; 8711562. ISSN: 0950-9232.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199311
ED Entered STN: 19940117
Last Updated on STN: 19950206
Entered Medline: 19931124
AB The reversible interaction of the **retinoblastoma** susceptibility gene product (Rb) with the cellular transcription factor E2F has recently been demonstrated. Activation of the **adenovirus E2a** promoter by the products of the viral E1a gene correlates with the ability of both early E1a proteins to sequester Rb, thereby releasing E2F from inactive complexes with this protein. The **E2a** promoter is also efficiently stimulated by a product (17.5 kDa) of the viral E4 gene. The specific interaction of this E4 protein with E2F results in the formation of complexes that bind cooperatively to the two neighboring E2F binding sites in the **E2a** promoter. We have previously shown that in undifferentiated F9 cells (F9EC) the **E2a** promoter is refractory to E2F-mediated activation by E1a, but not by E4. Using both band-shift and transfection experiments, we now demonstrate (i) that in F9EC cells the E4 product, in combination with E2F, recruits Rb into a stable multiprotein complex and (ii) that in these undifferentiated cells, as opposed to their differentiated counterpart, Rb is actively involved in the transcriptional stimulation of the **E2a** promoter by E4. Our results suggest that, depending on the cell state, Rb may behave either as a transcriptional activator (F9EC cells) or as a transcriptional inhibitor (differentiated F9 cells).

L6 ANSWER 8 OF 9 MEDLINE
AN 92278758 MEDLINE
DN 92278758 PubMed ID: 1534398
TI Complexes containing the **retinoblastoma** gene product recognize different DNA motifs related to the E2F binding site.
AU Ouellette M M; Chen J; Wright W E; Shay J W
CS Department of Cell Biology and Neuroscience, University of Texas Southwestern Medical Center, Dallas 75235-9039.
NC AG07992 (NIA)
CA50195 (NCI)
SO ONCOGENE, (1992 Jun) 7 (6) 1075-81.
Journal code: ONC; 8711562. ISSN: 0950-9232.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-X63096; GENBANK-X63097; GENBANK-X63905
EM 199207
ED Entered STN: 19920710
Last Updated on STN: 19920710
Entered Medline: 19920702
AB The **retinoblastoma** tumor-suppressor gene encodes a 105-kDa nuclear phosphoprotein (RB) that can associate with DRTF-1 and E2F. These two transcription factors can recognize the same DNA motif in the **adenovirus E2A** promoter and can bind to it by themselves or in association with RB. In the present report, we describe the use of CASTing (cyclic amplification and selection of targets) to determine the consensus binding site of RB-containing complexes. An anti-human RB antibody was used to isolate RB-containing complexes formed after mixing nuclear extracts obtained from human diploid fibroblasts with a pool of random oligonucleotides flanked with polymerase chain reaction (PCR) primers. After the immunoselection, the DNA was isolated, amplified, mixed

with fresh nuclear extract and reselected. After six CASTing cycles, the DNA was cloned and sequenced. We found that the highest affinity motifs recognized by RB-containing complexes are related to the E2F/DRTF-1 binding site and fall into three classes: TTTTCCCGCCAAAA, TTTTCCCGCCTTTTTT or TTTTCCCGCGCTTTTTT. Competition experiments revealed that these three classes are functionally equivalent to each other and to the E2F/DRTF-1 binding site in the **adenovirus E2A** promoter. Screening these sequences against a DNA database identified their presence in non-coding regions of many oncogenes, growth factor genes and in the RB gene itself.

L6 ANSWER 9 OF 9 MEDLINE
AN 92019798 MEDLINE
DN 92019798 PubMed ID: 1923506
TI Analysis of viral and cellular gene expression during progression and suppression of the transformed phenotype in type 5 **adenovirus** -transformed rat embryo cells.
AU Duigou G J; Su Z Z; Babiss L E; Driscoll B; Fung Y K; Fisher P B
CS Department of Neurological Surgery, Columbia University, College of Physicians and Surgeons, New York, New York 10032.
NC CA35675 (NCI)
CA43208 (NCI)
CA44754 (NCI)
+
SO ONCOGENE, (1991 Oct) 6 (10) 1813-24.
Journal code: ONC; 8711562. ISSN: 0950-9232.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199111
ED Entered STN: 19920124
Last Updated on STN: 19920124
Entered Medline: 19911118
AB Transformation of secondary Sprague-Dawley rat embryo (RE) cells with type 5 **adenovirus** (Ad5) results in morphologically transformed cells which can undergo a series of sequential changes resulting in enhanced expression of the transformed phenotype, a process termed progression. Selection for a progressed phenotype often occurs after growth in agar or tumor formation in nude mice, and this process is reversible following treatment of cells with 5-azacytidine. In the present study we have analyzed a series of clonal populations of Ad5-transformed RE cells representing different stages in a defined progression lineage. Progression was not associated with alterations in the steady-state levels of mRNA produced by the viral transforming genes, E1A and E1B, or the cellular gene, c-myc. In addition, the tumor-promoting agent 12-O-tetradecanoyl-phorbol-13-acetate (TPA), which induces expression of a progressed phenotype in Ad5-transformed RE cells, did not significantly alter the RNA transcription rates of the Ad5 E1A or E1B genes, the TPA-inducible gene TPA-S1 or the TPA-responsive genes Pro1 or protein kinase C. TPA did, however, increase by 1 h the steady-state level of c-fos mRNA, but this effect was similar in both progressed and unprogressed cells. Progression also did not involve a change in the RNA transcription rate of a number of cellular and viral genes, including actin, c-Ha-ras, c-myc, v-fos, erbB, TGF-alpha, TGF-beta, Pro-2, transin, TPA-R1, v-myb and c-mos, or other **adenovirus** genes in addition to E1A and E1B, including **E2A** and E4. Immunoblotting analysis using E1B polyclonal antiserum further indicated that progression was not associated with changes in the levels of an Mr 21,000 polypeptide encoded by E1B. Similarly, immunoprecipitation analysis with an Ad2 E1A monoclonal

antibody indicated similar levels of the Mr 55,000 and 48,000 E1A polypeptides, as well as coprecipitated proteins of Mr 300,000, 107,000 and 105,000 [which is the **retinoblastoma** (Rb) protein], in E11 and E11-NMT cells. Immunoprecipitation of cell lysates with a monoclonal antibody specific for the Mr 105,000 Rb protein further demonstrated that progression also was not associated with a change in the level or state of phosphorylation of the Rb protein. However, transfection of a human Rb gene (also containing a neomycin resistance gene) into Ad5-transformed RE cells was more inhibitory, with respect to formation of G418-resistant colonies, in unprogressed than in progressed Ad5-transformed RE cells.(ABSTRACT TRUNCATED AT 400 WORDS)

=> file uspatfull

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	4.50	4.65

FILE 'USPATFULL' ENTERED AT 17:43:02 ON 14 DEC 2001
CA INDEXING COPYRIGHT (C) 2001 AMERICAN CHEMICAL SOCIETY (ACS)

FILE COVERS 1971 TO PATENT PUBLICATION DATE: 13 Dec 2001 (20011213/PD)
FILE LAST UPDATED: 13 Dec 2001 (20011213/ED)
HIGHEST GRANTED PATENT NUMBER: US6249914
HIGHEST APPLICATION PUBLICATION NUMBER: US2001051434
CA INDEXING IS CURRENT THROUGH 13 Dec 2001 (20011213/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 13 Dec 2001 (20011213/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Apr 2001
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Apr 2001

>>> Page images are available for patents from 1/1/1998. Patents <<<
>>> and applications are typically loaded on the day of publication.<<<
>>> Page images are available for display by the following day. <<<
>>> Image data for the /FA field are available the following update.<<<

>>> Complete CA file indexing for chemical patents (or equivalents) <<<
>>> is included in file records. A thesaurus is available for the <<<
>>> USPTO Manual of Classifications in the /NCL, /INCL, and /RPCL <<<
>>> fields. This thesaurus includes catchword terms from the <<<
>>> USPTO/MOC subject headings and subheadings. Thesauri are also <<<
>>> available for the WIPO International Patent Classification <<<
>>> (IPC) Manuals, editions 1-6, in the /IC1, /IC2, /IC3, /IC4, <<<
>>> /IC5, and /IC (/IC6) fields, respectively. The thesauri in <<<
>>> the /IC5 and /IC fields include the corresponding catchword <<<
>>> terms from the IPC subject headings and subheadings. <<<

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s E1

'E1' NOT FOUND
The E# entered is not currently defined.

=> s E2A

L11 447 E2A

=> s retinoblast?

L12 1269 RETINOBLAST?

=> s l11 and l12

```
L13          61 L11 AND L12

=> s PER.C6

         931696 PER
          19054 C6
L14          13 PER.C6
                (PER(W)C6)

=> s l14 and l11

L15           7 L14 AND L11

=> s l14 and l13

L16           5 L14 AND L13

=> d l16 1-5 bib, ab


L16  ANSWER 1 OF 5  USPATFULL
AN      2001:185090  USPATFULL
TI      Packaging systems for human recombinant adenovirus to be used in gene
        therapy
IN      Fallaux, Frits Jacobus, Leiderdorp, Netherlands
        Hoeben, Robert Cornelis, Leiden, Netherlands
        Van Der Eb, Alex Jan, Oegstgeest, Netherlands
        Bout, Abraham, Moerkapelle, Netherlands
        Valerio, Domenico, Leiden, Netherlands
PA      IntroGene B.V., Leiden, Netherlands (non-U.S. corporation)
        Rijksuniversiteit, Leiden, Netherlands (non-U.S. corporation)
PI      US 6306652          B1   20011023
AI      US 1999-333820           19990615 (9)
RLI     Continuation of Ser. No. US 1997-793170, filed on 25 Mar 1997, now
        patented, Pat. No. US 5994128 Continuation of Ser. No. WO 1996-NL244,
        filed on 14 Jun 1996
PRAI    EP 1995-201611       19950615
        EP 1995-201728       19950626
DT      Utility
FS      GRANTED
EXNAM   Primary Examiner: Priebe, Scott D.; Assistant Examiner: Nguyen, Dave
        Trong
LREP    Trask, Britt & Rossa
CLMN    Number of Claims: 14
ECL     Exemplary Claim: 1
DRWN    28 Drawing Figure(s); 27 Drawing Page(s)
LN.CNT 1883
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB      Presented are ways to address the problem of replication competent
        adenovirus in adenoviral production for use with, for example, gene
        therapy. Packaging cells having no overlapping sequences with a
selected
        vector and are suited for large scale production of recombinant
        adenoviruses. A method of the invention produces adenovirus incapable
of
        replicating. The method includes a primary cell containing a nucleic
        acid based on or derived from adenovirus and an isolated recombinant
        nucleic acid molecule for transfer into the primary cell. The isolated
        recombinant nucleic acid molecule is based on or derived from an
        adenovirus, and further has at least one functional encapsidating
        signal, and at least one functional Inverted Terminal Repeat. The
        isolated recombinant nucleic acid molecule lacks overlapping sequences
        with the nucleic acid of the cell. Otherwise, the overlapping sequences
        would enable homologous recombination leading to replication competent
```

adenovirus in the primary cell into which the isolated recombinant nucleic acid molecule is to be transferred.

L16 ANSWER 2 OF 5 USPATFULL
AN 2001:116818 USPATFULL
TI Packaging systems for human recombinant adenovirus to be used in gene therapy
IN Fallaux, Frits J., Leiderdorp, Netherlands
Hoeben, Robert C., Leiden, Netherlands
Bout, Abraham, Moerkapelle, Netherlands
Valerio, Domenico, Leiden, Netherlands
van der Eb, Alex J., Oegstgeest, Netherlands
Schouten, Govert, Leiden, Netherlands
PA Introgene B.V., Leiden, Netherlands (non-U.S. corporation)
PI US 6265212 B1 20010724
AI US 1999-356575 19990719 (9)
RLI Continuation-in-part of Ser. No. US 1997-793170, filed on 25 Mar 1997, now patented, Pat. No. US 5994128
PRAI EP 1995-201611 19950615
EP 1995-201728 19950626
DT Utility
FS GRANTED
EXNAM Primary Examiner: Clark, Deborah J. R.; Assistant Examiner: Wilson, Michael C.
LREP Trask Britt
CLMN Number of Claims: 5
ECL Exemplary Claim: 1
DRWN 21 Drawing Figure(s); 20 Drawing Page(s)
LN.CNT 2294
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The problem of replication competent adenovirus in virus production is solved in that we have developed packaging cells that have no overlapping sequences with a new basic vector and, thus, are suited for safe large scale production of recombinant adenoviruses. One of the additional problems associated with the use of recombinant adenovirus vectors is the host-defense reaction against treatment with adenovirus. Another aspect of the invention involves screening recombinant adenovirus vector lots, especially those intended for clinical use, for the presence of adenovirus E1 sequences, as this will reveal replication
competent adenovirus, as well as revertant E1 adenoviruses. It is also an aspect of the present invention to molecularly characterize the revertants that are generated in the newer helper/vector combinations.

L16 ANSWER 3 OF 5 USPATFULL
AN 2001:78920 USPATFULL
TI Method for intracellular DNA amplification
IN Hoeben, Robert Cornelis, Leiden, Netherlands
Bout, Abraham, Moerkapelle, Netherlands
PA Introgene B.V., Leiden, Netherlands (non-U.S. corporation)
PI US 6238893 B1 20010529
AI US 1999-334765 19990616 (9)
RLI Continuation of Ser. No. US 793170, now patented, Pat. No. US 5994128
PRAI EP 1995-201611 19950615
EP 1995-201728 19950626
DT Utility
FS Granted
EXNAM Primary Examiner: Schwartzman, Robert A.
LREP Trask Britt
CLMN Number of Claims: 4
ECL Exemplary Claim: 1
DRWN 28 Drawing Figure(s); 27 Drawing Page(s)
LN.CNT 1908
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A method for intracellular amplification of DNA is disclosed. The method

includes providing a mammalian cell with a first nucleic acid sequence encoding functional adenoviral **E2A** and E2B gene products and with a second nucleic acid sequence encoding a linear DNA fragment to be amplified. The second nucleic acid sequence further has at least one functional adenoviral Inverted Terminal Repeat on a terminus and, in one embodiment where there is only a single ITR, a hairpin-like structure on the other terminus. This allows the linear DNA fragment to be acted upon by the adenoviral **E2A** and E2B gene products, thus intracellularly amplifying the linear DNA fragment, which can be extracted.

L16 ANSWER 4 OF 5 USPATFULL
AN 2000:27804 USPATFULL
TI Packaging systems for human recombinant adenovirus to be used in gene therapy
IN Bout, Abraham, Ar Moerkapelle, Netherlands
Hoeben, Robert Cornelis, Ex Leiden, Netherlands
PA IntroGene, b.v., Netherlands (non-U.S. corporation)
PI US 6033908 20000307
AI US 1997-892873 19970715 (8)
RLI Continuation of Ser. No. US 793170
PRAI EP 1995-201611 19950615
EP 1995-201728 19950626
DT Utility
FS Granted
EXNAM Primary Examiner: Campell, Bruce R.; Assistant Examiner: Nguyen, Dave Trong
LREP Rae-Venter Law Group, P.C.
CLMN Number of Claims: 14
ECL Exemplary Claim: 1
DRWN 28 Drawing Figure(s); 27 Drawing Page(s)
LN.CNT 2015
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention provides improved methods and products based on adenoviral materials which can advantageously be used in for instance gene therapy.
In one aspect an adenoviral vector is provided which has no overlap with a suitable packaging cell line which is another aspect of invention. This combination excludes the possibility of homologous recombination, thereby excluding the possibility of the formation of replication competent adenovirus. In another aspect an adenovirus based helper construct which by its size is incapable of being encapsidated. This helper virus can be transferred into any suitable host cell making it a packaging cell. Further a number of useful mutations to adenoviral based materials and combinations of such mutations are disclosed, which all have in common the safety of the methods and the products, in particular avoiding the production of replication competent adenovirus and/or interference with the immune system. Further a method of intracellular amplification is provided.

L16 ANSWER 5 OF 5 USPATFULL
AN 1999:155512 USPATFULL
TI Packaging systems for human recombinant adenovirus to be used in gene therapy
IN Fallaux, Frits Jacobus, Be Leiderdorp, Netherlands
Hoeben, Robert Cornelis, Ex Leiden, Netherlands
Van der Eb, Alex Jan, Tw Oegstgeest, Netherlands

Bout, Abraham, Ar Moerkapelle, Netherlands
Valerio, Domenico, Ez Leiden, Netherlands
PA IntroGene B.V., Leiden, Netherlands (non-U.S. corporation)
PI US 5994128 19991130
WO 9700326 19970103
AI US 1997-793170 19970325 (8)
WO 1996-NL244 19960614
19970325 PCT 371 date
19970325 PCT 102(e) date
PRAI EP 1995-201611 19950615
EP 1995-201728 19950626
DT Utility
FS Granted
EXNAM Primary Examiner: Campell, Bruce R.; Assistant Examiner: Nguyen, Dave Trong
LREP Trask, Britt & Rossa
CLMN Number of Claims: 20
ECL Exemplary Claim: 1
DRWN 21 Drawing Figure(s); 27 Drawing Page(s)
LN.CNT 2109
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Presented are ways to address the problem of replication competent adenovirus in adenoviral production for use with, for example, gene therapy. Packaging cells having no overlapping sequences with a selected vector and are suited for large scale production of recombinant adenoviruses. A system for use with the invention produces adenovirus incapable of replicating. The system includes a primary cell containing a nucleic acid based on or derived from adenovirus and an isolated recombinant nucleic acid molecule for transfer into the primary cell. The isolated recombinant nucleic acid molecule is based on or derived from an adenovirus, and further has at least one functional encapsidating signal, and at least one functional Inverted Terminal Repeat. The isolated recombinant nucleic acid molecule lacks overlapping sequences with the nucleic acid of the cell. Otherwise, the overlapping sequences would enable homologous recombination leading to replication competent adenovirus in the primary cell into which the isolated recombinant nucleic acid molecule is to be transferred.